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EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	PAPER NUMBER
1636	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,769	PILLARISETTI ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *14-17 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18-25 and 27-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/12/04; 01/31/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I in the reply filed on 08/08/07 is acknowledged. Applicant's election of species Insulin and IL-6 without traverse in the reply is also acknowledged.

2. Claims 14-17 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 08/08/07.

For the purposes of prosecution the following is defined:

3. The specification defines "cell matrix signaling pathway (CMS) induced genes":

4. The cell matrix signaling pathway (CMS pathway) as used herein means the sophisticated communication and feedback between endothelial cells and smooth muscle cells. The endothelial cells form the outer lining of the blood vessel and are believed to perform a gatekeeper function. These cells determine the types of molecules that are transported from blood to the tissues. Underlying the endothelial cells are the smooth muscle cells which provide mechanical strength to the blood vessel and are essential to the overall integrity of the blood vessel. Both the endothelial cells and the smooth muscle cells, manufacture and secrete molecules into the space surrounding them to form a matrix or scaffold that holds the blood vessel together.
5. The information system for endothelial cells and smooth muscle cells is based upon molecules secreted into the matrix. These messengers dictate the growth of these cells, the movement of these cells, and the overall function (or dysfunction) of these cells. This pathway controls the function of the blood vessels. Through control of blood vessels, this pathway controls the function of the surrounding tissues. The location of the affected blood vessel within the body determines which of a variety of tissue functions can be effected (paragraphs 0032-0033).

6. Brooks et al (characterization of release of basic fibroblast growth factor from bovine retinal endothelial cells in monolayer cultures. Biochemistry Journal, 1991. 276:113-120) teaches that incubation of endothelial cultures in the presence of serum releases fibroblast growth factor into the media (see abstract, and figure 2).

7. Axel et al (Paclitaxel Inhibits Arterial Smooth Muscle Cell proliferation and Migration In vitro and In Vivo Using Local Drug Delivery, Circulation, 1997:96:636-645) teaches that insulin, epidermal growth factor, fibroblast growth facts, PDGF and serum influence have growth stimulatory effects and proliferative effect on smooth muscle cells in vitro and in vivo and interfere with microtubule formation (page 643, column II).

8. Ribozyme is not defined in the instant specification. Ribozyme: A ribonucleic acid molecule that can catalyze specific biochemical reactions especially in the processing of some RNA. ribozyme. (1992). In Academic Press Dictionary of Science and Technology. Retrieved October 22, 2007, from http://www.credoreference.com/entry/3152511ribozyme. (1992). In Academic Press Dictionary of Science and Technology.

Specification

9. The abstract of the disclosure is objected to because the abstract is not grammatically correct. The abstract recites the phrase "to capture the ceil-cell and cell-matrix communications that are operative in normal and diseases conditions" and should read "diseased" or "disease". Correction is required. See MPEP § 608.01(b).

10. The use of the trademark PATHWAYS software has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-10, 24, 27-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,900,041 in view of Axel et al (Paclitaxel Inhibits Arterial Smooth Muscle Cell

proliferation and Migration In vitro and In Vivo Using Local Drug Delivery, Circulation, 1997:96:636-645).

13. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s).

14. The MPEP states, at §804, that:

15. [t]he specification can always be used as a dictionary to learn the meaning of a term in the patent claim. In re Boylan, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in *Vogel* recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

16. Portions of the instant claims are more narrowly drawn than the corresponding patented claims. However, the portion of US Patent 6,900,041 that supports claims 1-10, 24, 27-30 defines the patented invention includes embodiments which possess each of the narrower limitations of monocultures of endothelial cells and smooth muscle cells, as recited the instant claims. Thus, the inventions of the instant claims are not patentably distinct from those of respective patented claims 1-27. However, the patented claims do not recite a co-culture of endothelial cells and smooth muscle cells.

17. Claims 1-10, 24, 27-30 of the instant application read on methods of testing compounds on cell cultures of endothelial cells and smooth muscle cells in monocultures and co-cultures in response to a variety of stimuli and test compositions. While the instant claims are drawn to co-cultures, and the claims of Cahoon et al are only drawn to monocultures along with the specific examples of Cahoon are drawn to monocultures of endothelial cells and smooth muscle cells (see examples), Axel et al teaches that co-cultures of cells comprising smooth muscle cells and endothelial cells are improved in vitro methodologies that more accurately reproduce cell-cell interactions in vitro (page 637, column I). Further, the claims of Cahoon et al utilize the administration of insulin, AGE, and measure interleukin-6 in the methodologies. Thus it would have been obvious to the skilled artisan to modify the claims of Cahoon et al wherein only two cell cultures are analyzes, with the teaching of Axel et al, that the in vivo environment is better analyzed using a co-culturing system of endothelial cells and smooth muscle cell cultures because All of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention ((See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)). Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). In the instant case, the Office records do not indicate ownership of the instant application. Therfore, it is presently assumed that the instant application and the '041 patent are commonly owned. As discussed above, the '041 patent would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claim Rejections - 35 USC § 112

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claims 18-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 18-22 read on a method utilizing a genus of compounds identified by the process of claim 7, but does not require any active steps of practicing the method of claim 7. Thus, any compound that would be identifiable by the same methodology of claim 7, even if not identified by actively practicing claim 7 would inherently read on the compound of the claims.

20. The claim appears to be a reach through type claim wherein applicants are claiming an identified or identifiable inhibitor and method of use. The claims therefor read on a genus of inhibitors and methods of use.

21. The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

22. In the instant case, applicants have provided no examples of any test compounds actually identified by the methodology. Applicants only test different vascular disease stimuli in the examples (Tnf-alpha, Interleukin –1, AGE and insulin). Applicants do not disclose how the compound identified regulate CMS pathway induced genes . Applicants have not provided any clues to specific characteristics of the modulators than those in the prior art. There millions of potential inhibitors, as indirect or direct modulators of CMS pathway genes.

23. The skilled artisan would be unable to describe, or envision, any specific modulator of CMS genes based upon the teaching of the instant specification. The skilled artisan would therefore conclude that the applicants have not provided any examples of any modulators of CMS genes.

24. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

25. Claim 13 recites the limitation "the protein product" in claim 10. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

26. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

27. Claims 1, 4-7, 10, 18-25, and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Axel et al (Paclitaxel Inhibits Arterial Smooth Muscle Cell proliferation and Migration In vitro and In Vivo Using Local Drug Delivery, Circulation, 1997:96:636-645). Claims 1, 4-7, 10, 18-25 and 27 read on a method of identifying cell matrix signaling pathway induced genes that are modulated during vascular or proliferative diseases and related disorder by adding a vascular disease stimuli to a first culture or endothelial cells, adding a stimuli to a second cell culture of smooth muscle cells, and adding a stimuli to a third culture of cells comprising a co-culture of endothelial cells and smooth muscles cells, measuring the amount of a vascular disease marker, in all cultures, and comparing each of the markers measured to each other, and to a culture of untreated control cultures. The method is further limited wherein the smooth muscles cells are layered over the co-culture in a specific ratio, including a 1:1 ratio, and wherein a test compound is administers with the individual and co-cultures cells. The test compound is limited to a small organic molecule. The claims further read on a method of treating or preventing inflammation comprising administering a effecting amount of a pharmaceutical composition comprising one or more compounds identified as a test compound, in a diluents, that is administered intravenously. Furthermore, claim 22 read on a method of treating a subject for inflammation comprising the administration of a compound identified using the methodology above, wherein the pharmaceutical composition is administered in combination with other therapeutic agents.

28. Axel et al teaches a method of investigating the effect of the anti-proliferation drug Paclitaxel on in vitro monocultures of endothelial cell cultures, monocultures of smooth muscle cell cultures, and cocultures of endothelial cells and smooth muscle cells in vitro (see abstract, and page 639). Axel teaches that the cells are grown in the presence of serum, which inherently results in the production and secretion of vascular disease stimuli into the culture media for all cultures and even coincubated the cells with a variety of growth factors in cultures of smooth muscle cells (see page 637). He teaches that the cells are co-cultures at a specific ratio of 1:1, and that the smooth muscle cells are layered over the endothelial cells (see page 637, transfilter coculture system section). He teaches that the monocultures and cocultures exposed to vascular disease stimuli and paclitaxel are all compared to each other, and to an ethanol control cell populations (see page 639-640). Axel then determined the effect of the vascular disease stimuli and paclitaxel by staining for beta-tubulin, vimentin, smooth muscle actin and von-willabrand factor which read on vascular disease markers (page 638). Absent evidence to the contrary, Paclitaxel reads on a small organic molecule or small in organic molecule.

29. Claims 18 and 23 read on a method of administering any agent identified using the methodology of claim 7. Thus, the preamble of claim 18, "a method of treating or preventing inflammation" does not bear any patentable weight, as claim 7 does not require hat the agent identified is involved in the inflammatory pathway, only that it regulates CMS pathway induced genes. Therefore, any compound that would be identifiable by the same methodology of claim 7 would inherently also be able to treat

inflammation as would regulate CMS induced genes. Axel then teaches that Paclitaxel is administered to a subject by administering the Paclitaxel that has been diluted into a NaCl solution, thus broadly reading on the administration of the compound with other therapeutic agents as NaCl is an agent commonly used in therapeutic methods (see page 638). The Paclitaxel is administered intravenously in a catheter to the animals (see page 638). However, he does state that Paclitaxel is a good candidate to local drug therapy of excessive smooth muscle cell proliferation in restenosis after balloon angioplasty or stent implantation (page 636), which reads on a method of treating inflammation. He also states that the exact effect of Paclitaxel on endothelial cells and or smooth muscle cells is unknown (page 636).

30. Claims 24 and 25 read on a method of identifying compounds that regulate CMS pathway induced gene protein product *activity,* by identifying a test compound that regulated the activity to a protein product, and then administering the test compound to a patient. Axel teaches that Paclitaxel influences microtubule polymerization, and measures for by staining for beta-tubulin, vimentin, smooth muscle actin and von-willabrand factor which reads on vascular disease markers (page 638) and compares these to microtubule assembly patterns, thus determining the activity of the CMS induced pathway genes (see pages 640-641, figures 6-7).

31. Thus Axel teaches the claimed invention.

Claim Rejections - 35 USC § 103

32. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

33. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

34. Claims 2, 3, 8, 9, 11-13, 28-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Axel et al (Paclitaxel Inhibits Arterial Smooth Muscle Cell proliferation and Migration In vitro and In Vivo Using Local Drug Delivery, Circulation, 1997:96:636-645) as applied to claims 1, 7 and 24 above, and further in view of Cahoon et al (US Patent 6,900,041). Claims 2-3, 8-9, 11-13, and 28-30 read on a method of identifying a compound that affects a cell matrix pathway induced gene, utilizing monocultures of endothelial cells, smooth muscle cells, and co-cultures of the endothelial cells and smooth muscle cells, wherein a vascular disease stimulant is added to the cultures, and

a vascular disease marker is measured after addition of the stimulant and/or the test compound, wherein the stimuli is AGE, insulin, IL-1beta, or TNF-alpha, and the disease marker is IL-6, IP-10, MIG, I-TAC, VCAM-1, MCP-1. The method is further limited wherein the stimuli is a single disease stimulus.

35.

36. The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

37. Axel et al teaches a method of identifying a compound that affects a cell matrix pathway induced gene, utilizing monocultures of endothelial cells, smooth muscle cells, and co-cultures of the endothelial cells and smooth muscle cells, wherein a vascular

disease stimulant is added to the cultures, and a vascular disease marker is measured after addition of the stimulant and/or the test compound, and teaches the administration of the compound to treat inflammation (see above). Axel teaches that the stimuli is the result of various stimuli as a result of incubation with serum, or the administration of a single stimuli to monocultures of Smooth muscle cells with PDGF, FGF or thrombin (see page 637). Axel teaches that the co-culture system he employs imitates the complexity of in vivo cell-cell interactions which influence the efficacy of antiproliferation drugs (page 637, column I). Axel teaches that insulin, epidermal growth factor, fibroblast growth facts, PDGF and serum influence have growth stimulatory effects and proliferative effect on smooth muscle cells in vitro and in vivo and interfere with microtubule formation (page 643, column II). However, Axel does not teach that the stimuli is AGE, insulin, IL-1beta, or TNF-alpha, and the disease marker is IL-6, IP-10, MIG, I-TAC, VCAM-1, MCP-1, or that the method is further limited wherein the stimuli is a single disease stimulus to all three cell cultures.

38. Cahoon et al teaches methods of identifying an treating inflammatory diseases which modulate glycogen synthase kinase (see abstract). Glycogen synthase kinase reads on a cell matrix pathway induced gene as evidenced by figure 5. The methodology he employs utilizes the effect of adding insulin, AGE and/or TNF-alpha or insulin to individual monocultures of endothelial cells and smooth muscle cells, and measure the expression of interleukin –6 and glycogen synthase kinase activity (see examples 1-2). He further teaches that glycogen synthase kinase activity is measured in response to incubation with a test compound comprising antisense nucleic acids

directed towards glycogen synthase kinase and remeasures the markers (see examples 6, and figures 7 and 8). He further teaches that modulators of glycogen synthase kinase include nucleic acids which decrease transcription of the glycogen synthase kinase gene, and that they can target the 5' end of the genes including regulatory regions and promoter regions (column 8 line 52 through column 9, line 35). Additionally inhibitors inhibit the glycogen synthase kinase "act directly upon GSK-3beta" which reads on binding to the glycogen synthase kinase protein directly., The polynucleotide inhibitors can directly interfere with translation (page 9, lines 19-35), which reads on a ribozyme as defined above.

39.

40. It would have been obvious to the skilled artisan to combine the teachings of Axel et al a method of identifying a compound that affects a cell matrix pathway induced gene, utilizing monocultures of endothelial cells, smooth muscle cells, and co-cultures of the endothelial cells and smooth muscle cells, wherein a vascular disease stimulant is added to the cultures, and a vascular disease marker is measured after addition of the stimulant and/or the test compound, and teaches the administration of the compound to treat inflammation with the teaching of Cahoon et on the investigation of specific single stimulations and markers such as insulin, tnf-alpha, and interleukin 6, and test compounds comprising ribozymes and antisense polynucleotides directed at the 5' region of the target CMS gene because Axel teaches his co-culture system is an improved system that better replicates the in vivo environment, and the methodology of Cahoon can be used to investigate new compounds treatment for any inflammatory or

proliferation disease and that modifications can be made to his invention (column 9, lines 45-55). Co-culture systems of endothelial cells and smooth muscle cells were well known in the art, insulin, and TNf-alpha were known stimulants of vascular and proliferative diseases, and IL-6 was a well known marker of inflammatory responses. All of the claimed elements were known in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable result to one of ordinary skill in the art at the time of the invention ((See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007)). Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

Conclusion

41. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kam/10/22/07

/Daniel M. Sullivan/
Primary Examiner
Art Unit 1636